JC14 Rec'd PCT/PTO 19 DEC 2001

(1390 REV. 5-93) US DEPT. C[redacted]ERCE PATENT & TRADEMARK OFFICE

ATTORNEY'S DOCKET NUMBER
111504

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

U.S. APPLICATION NO.
(if known, sec 37 C.F.R.1.5)
10/018469

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/FR00/01848	June 30, 2000	July 16, 1999

TITLE OF INVENTION
NEEDLELESS SYRINGE OPERATING WITH A DEVICE GENERATING A SHOCK WAVE THROUGH A WALL

APPLICANTS FOR DO/EO/US
Patrick ALEXANDRE, Pierre BRUNET, Brigitte CAGNON, Claude MIKLER

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.

2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.

3. ☒ This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).

4. ☒ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.

5. ☒ A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. ☒ is transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☐ has been transmitted by the International Bureau.
   c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US)

6. ☒ A translation of the International Application into English (35 U.S.C. 371(c)(2)).

7. ☐ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☐ have been transmitted by the International Bureau.
   c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ☐ have not been made and will not be made.

8. ☐ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).

9. ☐ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).

10. ☒ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371 (c)(5)).

Items 11. to 16. below concern other document(s) or information included:

11. ☒ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.

12. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.

13. ☒ A FIRST preliminary amendment.

    ☐ A SECOND or SUBSEQUENT preliminary amendment.

14. ☐ A substitute specification.

15. ☐ Entitlement to small entity status is hereby asserted.

16. ☐ Other items or information:

531 Rec'd PCT/ 19 DEC 2001

U.S. APPLICATION NO. (if known, see 37 C.F.R. 1.5) 10/018469	INTERNATIONAL APPLICATION NO. PCT/FR00/01848	ATTORNEY'S DOCKET NUMBER 111504

17. ☒ The following fees are submitted:	CALCULATIONS	PTO USE ONLY
Basic National fee (37 CFR 1.492(a)(1)-(5)):		
Search Report has been prepared by the EPO or JPO $890.00		
International preliminary examination fee paid to USPTO (37 CFR1.482) $710.00		
No international preliminary examination fee paid to USPTO (37 CFR 1.482) but international search fee paid to USPTO (37 CFR 1.445(a)(2)) $740.00		
Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO.....$1,040.00		
☒ International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(2)-(4) .....$ 100.00		
ENTER APPROPRIATE BASIC FEE AMOUNT =	$890.00	
Surcharge of $130.00 for furnishing the oath or declaration later than ☒ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492(e)).	$	

Claims	Number Filed	Number Extra	Rate		
Total Claims	10- 20 =	0	X $ 18.00	$	
Independent Claims	1- 3 =	0	X $ 84.00	$	
Multiple dependent claim(s)(if applicable)			+ $280.00	$	
TOTAL OF ABOVE CALCULATIONS =				$890.00	
Reduction by 1/2 for filing by small entity, if applicable.			-	$	
SUBTOTAL =				$890.00	
Processing fee of $130.00 for furnishing the English translation later than ☐ 20 ☐ 30 month from the earliest claimed priority date (37 CFR 1.492(f)).			+	$	
TOTAL NATIONAL FEE =				$890.00	
				Amount to be refunded	$
				Charged	$

a. ☒ Check No. 126130 in the amount of $890.00 to cover the above fees is enclosed.

b. ☐ Please charge my Deposit Account No. _____ in the amount of $_____ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. ☒ The Director is hereby authorized to charge any additional fees which may be required, or credit any overpayment, to Deposit Account No. 15-0461. A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:
OLIFF & BERRIDGE, PLC
P.O. Box 19928
Alexandria, Virginia 22320

NAME: William P. Berridge
REGISTRATION NUMBER: 30,024

NAME: Joel S. Armstrong
REGISTRATION NUMBER: 36,430

Date: December 19, 2001

(1390 Rev.10-00)

PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of

Patrick ALEXANDRE, Pierre BRUNET,
Brigitte CAGNON, Claude MIKLER

Application No.: U.S. National Stage
of PCT/FR00/01848

Filed: December 19, 2001 Docket No.: 111504

For: NEEDLELESS SYRINGE OPERATING WITH A DEVICE GENERATING A SHOCK WAVE THROUGH A WALL

PRELIMINARY AMENDMENT

Director of the U.S. Patent and Trademark Office
Washington, D. C. 20231

Sir:

Prior to initial examination, and after entry of the annexes to the IPER, please amend the above-identified application as follows:

IN THE CLAIMS:

Please replace claims 3, and 5-9 as follows:

3. (Amended) The needleless syringe as claimed in claim 1, characterized in that the shock wave generator device (3) produces a plane shock wave on the upstream face (5) of the fixed barrier (4).

5. (Amended) The needleless syringe as claimed in claim 1, characterized in that each cavity (7) has a form of revolution about an axis parallel to the direction of propagation of the shock wave.

6. (Amended) The needleless syringe as claimed in claim 1, characterized in that a plurality of cavities are distributed on the downstream face (6) of said barrier (4).

7. (Amended) The needleless syringe as claimed in claim 1, characterized in that the shock wave on the upstream face (5) of the fixed barrier (4) is produced by a weight which impacts said barrier (4).

8. (Amended) The needleless syringe as claimed in claim 1, characterized in that the device (3) generating a shock wave on the upstream face (5) of the fixed barrier (4) comprises a detonating pyrotechnic charge.

9. (Amended) The needleless syringe as claimed in claim 1, characterized in that the length of the application guide (8) is between 1 and 8 times the diameter of the fixed barrier (4) and preferably between 2 and 5 times said diameter.

REMARKS

Claims 1-10 are pending. By this Preliminary Amendment, claims 3 and 5-9 are amended to eliminate multiple dependencies. Prompt and favorable examination on the merits is respectfully requested.

The attached Appendix includes marked-up copies of each rewritten claim (37 C.F.R. §1.121(c)(1)(ii)).

Respectfully submitted,

William P. Berridge
Registration No. 30,024

Joel S. Armstrong
Registration No. 36,430

JAO:JSA/cmm

Attachment: Appendix

Date: December 19, 2001

OLIFF & BERRIDGE, PLC
P.O. Box 19928
Alexandria, Virginia 22320
Telephone: (703) 836-6400

DEPOSIT ACCOUNT USE AUTHORIZATION
Please grant any extension necessary for entry;
Charge any fee due to our Deposit Account No. 15-0461

APPENDIX

Changes to Claims:

The following are marked-up versions of the amended claims:

3. (Amended) The needleless syringe as claimed in claim 1 ~~either of claims 1 and 2~~, characterized in that the shock wave generator device (3) produces a plane shock wave on the upstream face (5) of the fixed barrier (4).

5. (Amended) The needleless syringe as claimed in claim 1 ~~either of claims 1 and 4~~, characterized in that each cavity (7) has a form of revolution about an axis parallel to the direction of propagation of the shock wave.

6. (Amended) The needleless syringe as claimed in claim 1 ~~either of claims 1 and 4~~, characterized in that a plurality of cavities are distributed on the downstream face (6) of said barrier (4).

7. (Amended) The needleless syringe as claimed in claim 1 ~~one of claims 1 to 3~~, characterized in that the shock wave on the upstream face (5) of the fixed barrier (4) is produced by a weight which impacts said barrier (4).

8. (Amended) The needleless syringe as claimed in claim 1 ~~one of claims 1 to 3~~, characterized in that the device (3) generating a shock wave on the upstream face (5) of the fixed barrier (4) comprises a detonating pyrotechnic charge.

9. (Amended) The needleless syringe as claimed in claim 1 ~~one of the preceding claims~~, characterized in that the length of the application guide (8) is between 1 and 8 times the diameter of the fixed barrier (4) and preferably between 2 and 5 times said diameter.

NEEDLELESS SYRINGE OPERATING WITH A DEVICE GENERATING A SHOCK WAVE THROUGH A WALL.

The present invention is in the field of needleless syringes used for intradermal, subcutaneous or intramuscular injections of various active principles for therapeutic use in human or veterinary medicine.

Many types of needleless syringes for injecting liquid active principles have been known since 1945. In these devices, the liquid active principle is delivered, via a nozzle comprising at least one orifice, by a piston or by the deformation of a flexible envelope containing said liquid, said flexible envelope being connected to the nozzle. The injection pressure is obtained either by the release of an initially compressed spring or by the release of a gas stored under pressure, as is described in US Patent 3,788,315. Other subcutaneous injection devices use a pyrotechnic charge generating gas to propel a piston which delivers the liquid to be injected, and US Patent 3,802,430 illustrates such a technique for generating propellant gas.

For injecting solid active principles in the form of a dry powder, needleless syringes use different means to accelerate the particles of said active principle, and mention must be made of patent application WO 94/24263

which describes a needleless syringe in which the particles of the active principle are entrained by a gas flow at high speed, by means of a compressed gas being released through a tubing. Despite the use of a long tubing, a dispersed cloud of particles is produced, which suggests that there is a low bioavailability. Auxiliary devices also have to be used to dissipate the blast effect and noise of the gas jet. Finally, the reliability of the system depends on that of the device used for storing the gases under pressure.

In another technical field, US Patent 4,945,050 describes the principle of a laboratory apparatus for bombarding a cell culture with metal microparticles coated with various biological substances for purposes of gene transfection. Different means are used in particular to transfer the kinetic energy of a projectile impacting a barrier to the particles arranged on the projectile or on this barrier and to cause these particles to penetrate into the cell culture. This laboratory apparatus operates under a vacuum and uses very dense neutral microparticles to increase the kinetic energy (microparticles of gold or of tungsten), which excludes any application or any transposition as a needleless syringe, especially since it produces a cloud of particles in order to reach the largest possible number of cells.

One of the objects of the invention is to overcome the disadvantages affecting needleless syringes permitting injection of powdered active principle. Another object of the present invention is to make available a more universal syringe which can be used for injection not only of powdered active principles but also of active principles which are liquid, or in suspension in a liquid, or in the form of gel. The transformation of the initial volume of the active principle and its streamlining at the moment of penetration into the skin are obtained by an effect of reversal and focusing which has been discovered and which has been observed in the case of liquids, gels and powders.

The present invention relates to a needleless syringe for injecting active principle for therapeutic use, comprising, from upstream to downstream, a propelling system, the active principle, and an application guide for applying said syringe to the skin of the subject to be treated, this syringe being such that, on the one hand, the propelling system consists of a shock wave generator device and, on the other hand, the active principle is arranged in at least one blind cavity of the downstream face of a barrier continued by the application guide. The barrier in fact has two opposite faces, namely an upstream one, situated toward the shock wave generator device, and another, the

downstream one, situated toward the application guide.

The upstream face of the barrier is substantially plane and transverse. The downstream face of the fixed barrier comprises at least one blind cavity, this cavity thus having an opening only on the downstream face of the fixed barrier and not opening out on the upstream face, thereby providing a thickness sufficient to resist the shock wave.

The shock wave generator device advantageously produces a plane shock wave on the upstream face of the fixed barrier. The plane shock wave produced on the upstream face of the fixed barrier propagates through this barrier and violently ejects the active principle from each of the cavities where it was arranged. Unexpectedly, the active principle thus accelerated at very high speed is able to regroup in the form of a central jet of small diameter which will then penetrate into the skin of the subject. Each jet corresponds to a cavity and has a streamlined shape at its downstream end once the distance traveled by this jet corresponds to several diameters from the fixed barrier. It should be noted that the phenomenon of ejection in the form of jets is fully effective when the shock wave is plane at the moment when it reaches the cavities. This does not exclude the possibility that the shock wave produced on the upstream face may not be strictly plane and may

have a slight curvature, which will be eliminated upon propagation in the barrier.

This phenomenon of shaping into a streamlined jet of active principle starting from the principle initially stored in globular form, in all or part of a cavity subjected to a shock wave, can be likened to the jets of substance which result from the detonation of explosive charges having a concave downstream face covered by a metal foil. Such explosive charges, referred to as "hollow charges", make it possible to obtain streamlined shards at high temperature which are propelled at speeds of the order of 8000 meters per second and are capable of piercing armored plating of up to 1 meter in thickness. However, the phenomenon employed in the present invention is of an entirely different nature since the active principle must not in practice experience any increase in temperature and propulsion speeds of the order of 600 to 1000 meters per second are entirely sufficient to permit an injection through the epidermis. In contrast to the explosive charges forming a central jet of substance, the explosive must not be in contact with the substance to be ejected and must be separated by a resistant barrier which ensures a good propagation of the shock wave, which barrier can be made, for example, of aluminum or steel. On account of the limited speed of ejection of the jet of active principle, it was

discovered that not only could the shock wave be obtained with a small quantity of explosive whose detonation is triggered by a microdetonator, but that this shock wave could be obtained by other means such as the propulsion of a weight which strikes the upstream face of the fixed barrier.

Advantageously, to obtain a streamlined jet, each blind cavity of the fixed barrier has an opening transverse section which is at least equal to each transverse section of this cavity and preferably each cavity has a form of revolution about an axis parallel to the direction of propagation of the shock wave, with the aim of promoting the formation of a jet which is perfectly aligned on the axis of said cavity.

A cavity can preferably have, for example, a hemispherical, conical or frustoconical shape or can consist of a combination of these profiles.

According to an alternative embodiment, a plurality of cavities are distributed on the downstream face of the barrier. These cavities, which can have different shapes, are advantageously distributed uniformly on said surface.

The active principle is advantageously deposited at the bottom of the cavity and preferably fills the whole

cavity until it is flush with the plane part of the downstream face in which it is retained, for example, by means of a thin film. This is because digital simulations have shown that with such a configuration of filling, the diametrical dispersion of the jet is minimal.

The material used for the fixed barrier is chosen from the group of materials which do not give rise to the phenomenon of flaking under the action of a shock wave, such as, for example, metals. It is also chosen on the basis of its density and its acoustic impedance, in other words its ability to transmit the shock wave. It is in particular chosen as a function of the speed one wishes to communicate to the jet.

In a first embodiment, the shock wave on the upstream face of the fixed barrier is produced by the impact, on said upstream face, of a weight of suitable shape which is accelerated by an auxiliary device. The diameter of said weight is advantageously such that the air located between the weight and the fixed barrier is expelled without braking said weight, which is guided by suitable means. The acceleration of the weight is effected either by the release of a compressed spring or by the combustion of a pyrotechnic charge, or by the release of compressed gas.

In a second embodiment, the plane shock wave on the upstream face of the fixed barrier is produced by a shock wave generator which comprises a detonating pyrotechnic charge. The latter advantageously comprises a foil of explosive adjacent to the upstream face, said foil of explosive being triggered either at a point or over all or part of its surface by a microdetonator. This foil of explosive has a diameter substantially equal to that of the fixed barrier and comprises several tens of milligrams of an explosive such as TNT or a composite explosive with a high speed of detonation.

The application guide has a length which is such that it allows the active principle, during its ejection toward the skin, to regroup in the form of a streamlined jet. The length of the application guide is advantageously between 1 and 8 times the diameter of the fixed barrier and preferably between 2 and 5 times the diameter of the fixed barrier.

The application guide advantageously comprises a shock absorbing system which can be reduced to a simple flexible flange situated at its end bearing on the skin of the subject to be treated, or can consist of a telescopic application guide with an inner spring.

The present invention satisfactorily solves the problems posed and makes it possible, for example, to obtain, for a barrier of 5 mm diameter and 2 mm thickness, jets of diameters between 0.12 mm and 1.6 mm when use is made of ogival, substantially hemispherical or conical cavities, although in the case of conical cavities in particular it is advantageous if the downstream face of the active principle is plane and does not exceed 3 to 4 mm in diameter.

For a barrier with a diameter of 5 millimeters, a thickness of 3 millimeters and a hemispherical cavity of one millimeter radius, using an explosive pellet with a diameter of 3 millimeters and a thickness of 1 millimeter, it is possible to obtain a jet having a maximum diameter of 0.7 millimeter with a speed of ejection of 630 meters per second.

The major effect sought using the ejection device according to the invention is an attenuated effect referred to as "hollow charge" which translates into the formation of a streamlined jet composed of the particles of substance to be expelled, and driven, on its axis, at a very high speed which gives it a high force of penetration. The characteristics of this jet, namely its shape, its length, its dispersion and its speed of displacement are a function of the nature and

positioning of the generator of plane waves, the material constituting the part serving as barrier, and the geometry of the cavities in the downstream face serving to accommodate the particles. At a lower level, the general shape of the volume formed by the particles in each cavity also plays a role.

Advantageously, under the effect of the pyrotechnic charge, the barrier, although having been deformed, remains fixed in the syringe at its original position. According to another embodiment of the invention, when confronted by the same stress the barrier is displaced but remains trapped in the syringe without any possibility of being expelled.

The application guide is preferably made up of a hollow cylindrical body whose cross section is similar to that formed by the downstream face of the barrier and whose axis is perpendicular to said face. This guide is particularly recommended for optimizing the conditions for achieving a perpendicular impact on said surface.

According to a first embodiment of the invention, the particles form a mass of powder in each cavity. These particles are held in their seat by capillarity, by static electricity, by an adhesive surface state or by a membrane covering each cavity. Finally, any means of adhesion can be used, provided that it does not

interfere with the formation of the jet.

According to a second embodiment of the invention, the particles are bound to each other by a liquid which is fluid, viscous or in the form of a gel. In relation to this liquid, the particles of active principle can be either in suspension or in solution.

Advantageously, the trigger can be a push button which initiates the microdetonator by percussion.

The device according to the invention has the advantage of being efficient while having a simple and lightweight design which takes up little space. This is because the technique involving the formation of a jet using the hollow charge model allows particles to be projected in concentrated form and at very high speed from a device having a small number of components made of lightweight materials and arranged in a simple manner in relation to one another.

Moreover, a rapid dimensioning makes it possible to adapt the device to a wide range of situations, by acting in particular on the cross section of the jet, its dispersion, its length, its speed, and the number of jets to be expelled.

Furthermore, as the active principle is not set in motion by the release of the gases, there is no hissing effect. Nor is there any noise associated with the release of the gases to the outside, the noise only possibly originating from the impact of the weight on the barrier or from the functioning of the pyrotechnic charge, which are internal to the syringe.

The present invention will now be described in more detail with the aid of Figure 1 which shows a partial cross-sectional view of a syringe according to the invention and which can be used to describe two shock wave generators.

Figure 1 shows a view of a syringe 10 before use, the downstream end of this syringe 10 still being closed by a hermetic stopper 15 which ensures asepsis of the inner part of the application guide 8.

According to this Figure 1, the application guide 8 is continued inside the trigger tube 1 and comprises, from downstream to upstream, a threaded ring 16 which ensures the immobilization of a fixed barrier 4 on a shoulder of the guide, this shoulder forming a central opening in which the shock wave generator device 3 is placed, formed by a pellet of sensitive composite explosive, surmounted by a microdetonator which can be initiated by percussion. A weight 9 is able to slide in

the internal continuation of the application guide 8 and comprises a striker pin at its downstream end and a retainer groove in which there are engaged three balls 11 placed in radial perforations of this continuation. These balls 11 bear on the inner surface of the trigger tube 1 and immobilize the hollow weight percussion 9 surmounted by a spring 13 compressed between this weight 9 and the bottom of the trigger tube 1, this tube 1 being held in the initial position by a lower internal shoulder in contact with the application guide 8.

The powdered active principle fills a semi-ellipsoid cavity 7 situated on the downstream face 6 of the barrier 4, and this principle is held by means of a thin film secured on the fixed barrier 4 and wedged by the threaded ring 16.

In operation, after the stopper 15 has been removed and the freed end of the application guide 8 has been applied in contact with the area of the epidermis chosen for injection of the active principle, the trigger tube 1 is pressed in order to compress the spring 13 until the inner groove 12 of this tube 1 arrives at the level of the three balls 11 which spread apart radially and release the hollow percussion weight 9 whose downstream point will strike the microdetonator, causing the explosive pellet in contact

with the upstream face 5 of the fixed barrier 4 to explode. The plane shock wave thus generated will reach the cavity 7 and simultaneously provoke the rupture of the thin film and the ejection of the active principle on the basis of a phenomenon of reversal and focusing similar to the phenomenon employed in hollow charges. The hollow weight 9, the spring 13 and the material 14 then have the function of absorbing the effects behind the detonation, and the shock absorbing system 2 of the application guide 8 attenuates the effect of compression in front, this sensation of annular compression largely masking the pricking sensation resulting from the penetration of the streamlined jet of active product into the epidermis and dermis.

According to an alternative embodiment which can be described with reference to this same figure, the plane shock wave is not produced by an explosive in contact with the barrier 4 in which the blind cavity 7 is formed. This alternative (not shown) requires the use of a solid weight which is continued downstream by a cylindrical striking peen which can engage in the bore obtained by removing the explosive and the detonator so as to strike the fixed barrier 4 directly. In this alternative, the spring 13 is not useful and the material 14 must be replaced by a pyrotechnic gas generator which can be activated by an external means, the trigger tube 1 being completely integral with the

application guide 8 and comprising an internal sheath deformable at the level of the three balls 11. In operation, the initiation of the pyrotechnic gas generator ensures a pressure increase in the chamber between the trigger tube and the weight, until the pressure exerted on this weight causes the partial engagement of the three balls in the deformable sheath and frees this weight, of which the peen will strike the fixed barrier 4 and will generate a plane shock wave with which it is possible to obtain the formation of a streamlined jet of the active product initially stored in globular form in the blind cavity 7.

Claims

1. A needleless syringe (10) for injecting active principle and comprising, from upstream to downstream, a propelling system consisting of a shock wave generator device, a barrier comprising an upstream face (5) and a downstream face (6), said downstream face (6) having at least one blind cavity (7) in which the active principle is accommodated, and an application guide (8) for applying said syringe (10) to the skin of the patient to be treated, characterized in that, on the one hand, the barrier (4) is fixed and resistant to the shock wave and, on the other hand, said barrier (4) ensures a good propagation of the shock wave.

2. The needleless syringe as claimed in claim 1, characterized in that the barrier (4) has a substantially plane and transverse upstream face (5).

3. The needleless syringe as claimed in either of claims 1 and 2, characterized in that the shock wave generator device (3) produces a plane shock wave on the upstream face (5) of the fixed barrier (4).

4. The needleless syringe as claimed in claim 1, characterized in that each blind cavity (7) has an opening transverse section which is at least equal to each transverse section of this cavity (7).

5. The needleless syringe as claimed in either of claims 1 and 4, characterized in that each cavity (7) has a form of revolution about an axis parallel to the direction of propagation of the shock wave.

6. The needleless syringe as claimed in either of claims 1 and 4, characterized in that a plurality of cavities are distributed on the downstream face (6) of said barrier (4).

7. The needleless syringe as claimed in one of claims 1 to 3, characterized in that the shock wave on the upstream face (5) of the fixed barrier (4) is produced by a weight which impacts said barrier (4).

8. The needleless syringe as claimed in one of claims 1 to 3, characterized in that the device (3) generating a shock wave on the upstream face (5) of the fixed barrier (4) comprises a detonating

pyrotechnic charge.

9. The needleless syringe as claimed in one of the preceding claims, characterized in that the length of the application guide (8) is between 1 and 8 times the diameter of the fixed barrier (4) and preferably between 2 and 5 times said diameter.

10. The needleless syringe as claimed in claim 9, characterized in that the application guide (8) comprises a shock absorbing system (2).

Concerning point V

Reasoned statement according to Article 35(2) with regard to novelty, inventive activity and industrial applicability; citations and explanations supporting this statement

Reference is made to the following document:

D1: WO 96 25190 A (OXFORD BIOSCIENCES LTD; BELLHOUSE BRIAN JOHN (GB); BELL JOHN (GB)) 22 August 1996 (22.8.1996)

1. The subject of independent claim 1 satisfies the requirements regarding novelty and inventive activity, Article 33(2) and (3) PCT.

Document D1, which is considered the closest prior art, describes a needleless syringe for injection of active principle, comprising, from upstream to downstream, a propelling system consisting of a shock wave generator device, a barrier comprising a downstream face having at least one blind cavity in which the active principle is accommodated, and an application guide for said syringe,

from which the syringe forming the subject of claim 1 differs in that said barrier is fixed and resistant to the shock wave and said barrier ensures a good propagation of the shock wave.

The problem which the present invention sets out to solve can be considered as being that of forming more streamlined jets of solid active principle which have a high perforation capacity.

The problem is solved by said barrier which is fixed and resistant to the shock wave and is able to ensure a good transmission of the shock wave. The principle of focusing of the syringe is inspired by the "hollow charge" effect by which the shock wave produced on the upstream face of said fixed and resistant barrier propagates through the barrier and reaches the downstream face of the barrier. When the shock wave has reached the particles of active principle accommodated in the blind cavity situated in the downstream face of the barrier, these particles organize to form a convergent protuberance which changes into a streamlined jet when the shock wave has reached the downstream face of the barrier.

No document in the prior art discloses or renders evident the needleless syringe based on the "hollow charge" effect which includes a fixed and resistant barrier ensuring a good propagation of the shock wave in order to focus the jet of active principle.

2. Claims 2-10 are dependent on claim 1 and introduce additional characteristics of the needleless syringe defined by claim 1.

For this reason, claims 2-10 also satisfy the requirements under Article 33(2) and (3) PCT concerning novelty and inventive activity.

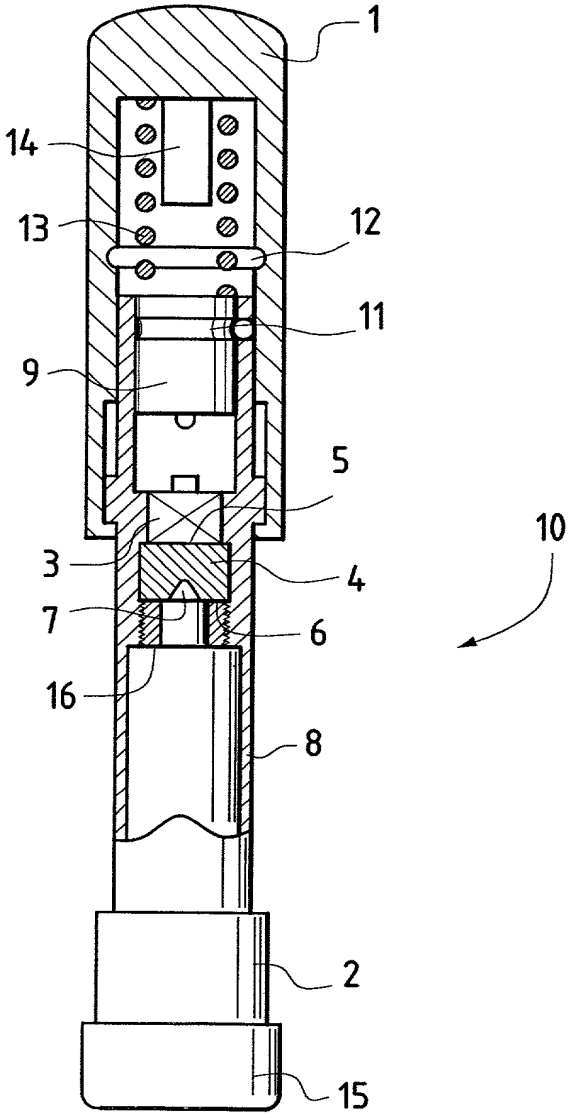

FIG.1

Docket No.: _____

B 1117 FCT

DECLARATION AND POWER OF ATTORNEY UNDER 35 USC §371(c)(4) FOR PCT APPLICATION FOR UNITED STATES PATENT

As a below named inventor, I hereby declare that:
my residence, post office address and citizenship are as stated below under my name;

I verily believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought, namely the invention entitled: Needleless syringe operating with a device generating a shock wave through a wall

described and claimed in international application number _____ filed _____.

I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose to the Office all information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations §1.56.

Under Title 35, U.S. Code §119, the priority benefits of the following foreign application(s) filed within one year prior to my international application are hereby claimed:

French Patent Application No 99 09255 filed on July 16, 1999

The following application(s) for patent or inventor's certificate on this invention were filed in countries foreign to the United States of America either (a) more than one year prior to my international application, or (b) before the filing date of the above-named foreign priority application(s):

I hereby appoint the following as my attorneys of record with full power of substitution and revocation to prosecute this application and to transact all business in the Patent Office:

James A. Oliff, Reg. No. 27,075; William P. Berridge, Reg. No. 30,024; Kirk M. Hudson, Reg. No. 27,562; Thomas J. Pardini, Reg. No. 30,411; Edward P. Walker, Reg. No. 31,450; Robert A. Miller, Reg. No. 32,771; Mario A. Costantino, Reg. No. 33,565; and Caroline D. Dennison, Reg. No. 34,494.

ALL CORRESPONDENCE IN CONNECTION WITH THIS APPLICATION SHOULD BE SENT TO OLIFF & BERRIDGE, PLC, P.O. BOX 19928, ALEXANDRIA, VIRGINIA 22320, TELEPHONE (703) 836-6400.

I hereby declare that I have reviewed and understand the contents of this Declaration, and that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

1 *Typewritten Full Name of Sole or First Inventor* Patrick (Given Name) _____ (Middle Initial) ALEXANDRE (Family Name)

2 **Inventor's Signature** _____

3 **Date of Signature** 13 Déc. 2001 (Month / Day / Year)

Residence: GRAY (City) _____ (State or Province) FRANCE (Country)

Citizenship: FRANCAISE

Post Office Address: 14 avenue de la Libération - 70100 GRAY
(Insert complete mailing address, including country) FRANCE

Note to Inventor: Please sign name on line 2 exactly as it appears in line 1 and insert the actual date of signing on line 3.

B 1117 PCT

PAGE 2 OF U.S.A. DECLARATION FORM
(Discard this page in a sole inventor application)

2-00

1 ***Typewritten Full Name of Second Joint Inventor (if any)*** Pierre (Given Name) — (Middle Initial) — BRUNET (Family Name)

2 **Inventor's Signature: PBRUNET

3 **Date of Signature: January (Month) 16 (Day) 2002 (Year)

Residence: LARDY (City) — FRANCE (State or Province / Country)

Citizenship: FRANCAISE FRX

Post Office Address: (Insert complete mailing address, including country) 17 rue Honville - 91510 LARDY, FRANCE

3-00

1 ***Typewritten Full Name of Third Joint Inventor (if any)*** Brigitte (Given Name) — (Middle Initial) — CAGNON (Family Name)

2 **Inventor's Signature: B. Cagnon

3 **Date of Signature: January (Month) 16 (Day) 2002 (Year)

Residence: BALLANCOURT (City) — FRANCE (State or Province / Country)

Citizenship: FRANCAISE FRX

Post Office Address: (Insert complete mailing address, including country) 24 Lotissement du Bois - 91610 BALLANCOURT, FRANCE

4-00

1 ***Typewritten Full Name of Fourth Joint Inventor (if any)*** Claude (Given Name) — (Middle Initial) — MIKLER (Family Name)

2 **Inventor's Signature:

3 **Date of Signature: December (Month) 19 (Day) 2001 (Year)

Residence: DIJON (City) — FRANCE (State or Province / Country)

Citizenship: FRANCAISE FRX

Post Office Address: (Insert complete mailing address, including country) 117 avenue du Drapeau - 21000 DIJON, FRANCE

1 ***Typewritten Full Name of Fifth Joint Inventor (if any)*** (Given Name) — (Middle Initial) — (Family Name)

2 **Inventor's Signature:

3 **Date of Signature: (Month) (Day) (Year)

Residence: (City) — (State or Province / Country)

Citizenship:

Post Office Address: (Insert complete mailing address, including country)

**Note to Inventors: Please sign name exactly as it appears and insert the actual date of signing.
This form may be executed only when attached to the first page of the Declaration and Power of Attorney form of the application to which it pertains.**